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DIALOG(R)File 5:Biosis Previews(R)

0015385135 BIOSIS NO.: 200510079635
%%%BAT%%% %%%mAb%%% induces lymphopoiesis in nude mice
AUTHOR: Hardy Britta (Reprint); Niv Yaron; Fadaeev Ludmila; Raiter Annat
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JOURNAL: International Immunology 17 (5): p615-619 MAY 05 2005
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The athymic nude mouse provides a powerful tool in the study of human tumors, as it enables growth of human tumors due to deficiencies in T cell functions. However, deficiencies in T cell functions might limit research on efficacy of immune modulators in cancer immunotherapy. %%%BAT%%% %%%mAb%%% mediates its anti-cancer activity through modulation of the immune system that involves both NK and T cells. We analyzed lymphocyte populations in blood 5 and 14 days following the injection of BAT antibody alone or following engraftment of human colon carcinoma cells. Our results demonstrate that BAT injection induced lymphopoiesis in the nude mouse. Percentage of CD3 cells increased up to 24%, CD4 cells up to 20% but no increase was found in CD8 T cells in BAT-injected nude mice. Injection of BAT 12 days post-tumor engraftment propagated CD3, CD4 and CD8 cells seen in the blood 5 days later but not seen in the blood 14 days post-BAT injection. It is possible that this decrease is associated with migration of the lymphocytes from the blood to the tumor sites in the livers. The percentage of CD56-positive NK cells increased (up to 18%) by BAT administration alone or post-tumor injection. The presence of tumors alone did not induce lymphopoiesis in the nude mice. Propagation and lymphopoiesis by %%%BAT%%% %%%mAb%%% might have future clinical implications.

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DIALOG(R)File 5:Biosis Previews(R)

0015319117 BIOSIS NO.: 200510013617
Cancer disease predictive diagnosis: BAT/CD3-positive lymphocytes in cancer patients

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JOURNAL: International Journal of Oncology 26 (4): p971-975 APR 05 2005
ISSN: 1019-6439
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: BAT is an immune-activating monoclonal antibody produced against Daudi cell membranes and selected for stimulating lymphocyte proliferation. The anti-tumor activity of BAT is related to its immunostimulatory properties. Both T and NK cells mediate the anti-tumor activity of BAT. CD4-positive T cells respond to BAT activation by proliferation and INF-gamma production. The aim of the study was to assess the probability that the BAT monoclonal antibody binding capacity to T cells is a marker for different cancers. Human peripheral blood T cells from colon, breast and prostate cancer patients, as well as healthy volunteer donors, were tested for the percentage of binding to %%%BAT%%% %%%mAb%%% (BAT/CD3 cells) by FACS analysis. All patients were tested before undergoing surgery or treatment, and their diagnosis was confirmed by histology. The results showed that the percentage of BAT monoclonal antibody binding to CD3-positive T cells in the peripheral blood was different in cancer patients with diverse tumor types. We found that lymphocytes from the blood of healthy donors contained 25% BAT/CD3 cells. In colon and breast cancer patients, a significant decrease to 13 and 11% of BAT/CD3 cells was found. In contrast, these cells increased > 50% in patients with prostate cancer. These findings may have a potential diagnostic significance and also assist in the evaluation of strategies for the therapeutic use of BAT for different cancer patients.

1/7/3
DIALOG(R)File 5:Biosis Previews(R)

0012816454 BIOSIS NO.: 200000534767
CD4+ T lymphocytes as a primary cellular target for %%%BAT%%% %%%mAb%%% stimulation
AUTHOR: Raiter Annat; Rodionov Galina; Novogrodsky Abraham; Hardy Britta (Reprint)
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JOURNAL: International Immunology 12 (11): p1623-1628 November, 2000 2000
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: BAT is a monoclonal antibody (mAb) produced against membranes of a human Burkitt lymphoma cell line (Daudi) that was selected for its ability to stimulate lymphocyte proliferation. BAT manifests anti-tumor

properties in mice bearing a variety of murine tumors. BAT also induced regression of human tumors inoculated into SCID mice that had been engrafted with human lymphocytes. The anti-tumor activity of BAT was related to its immune stimulatory properties. Previous data indicated that T lymphocytes and NK cells mediate in vivo the anti-tumor activity. In order to define the primary target cell for BAT stimulatory activity, the in vitro stimulatory effect of BAT on purified lymphocyte subpopulations was investigated. Human CD4+, CD8+ T cells and CD56+ NK cells were purified and their in vitro response to BAT was investigated. Results indicate that BAT selectively stimulated CD4+ cells as assessed by proliferation and secretion of IFN-gamma. FACS analysis has also revealed a selective increase in BAT antigen on CD4+ T cells that were cultured with BAT antibody. The effector cells that mediate BAT-induced tumor eradication may, however, be distinct from those that serve as the primary cellular target of the antibody. Cytokines such as IFN-gamma that are produced by CD4+ cells may be involved in activation of additional cell types that may be involved in tumor destruction.

1/7/4
DIALOG(R)File 5:Biosis Previews(R)

0010963297 BIOSIS NO.: 199799597357
A lymphocyte-activating monoclonal antibody induces regression of human tumors in severe combined immunodeficient mice
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JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (11): p5756-5760 1997 1997
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Monoclonal antibodies were raised against Daudi B-lymphoblastoid cell line membranes. An mAb (BAT) was selected for its ability to stimulate human and murine lymphocyte proliferation. BAT induced cytotoxicity in human and murine lymphocytes against natural killer cell-sensitive and -resistant tumor cell lines. A single intravenous administration of BAT to mice that had been inoculated with various murine tumors (e.g., B16 melanoma, 3LL carcinoma, and methylcholanthrene fibrosarcoma) resulted in striking antitumor effects as manifested by complete tumor regression and prolonged survival of the treated mice. BAT exhibited a diminished but significant antitumor effect in athymic nude mice, which are deficient in T lymphocytes, and in beige mice, which are deficient in NK cells. Furthermore, selective depletion of T or NK cells in mice reduced the response to the antitumor effect of BAT. These data indicate a dual role for T and NK cells in mediating the antitumor activity of BAT. We report here on the antitumor activity of %%%BAT%%% %%%mAb%%% on human tumor xenografts in mice. BAT demonstrated an antitumor effect in nude mice bearing human colon carcinoma (HT29) xenografts. It failed, however, to inhibit established lung metastases in severe combined immunodeficient (SCID) mice that had been inoculated (i.v.) with SK28 human melanoma. Engraftment of human lymphocytes into

SCID mice bearing human melanoma xenografts rendered them responsive to the antitumor effect of BAT. The efficacy of BAT in the regression of human tumors by activation of human lymphocytes indicates its potential clinical use.

1/7/5
DIALOG(R)File 5:Biosis Previews(R)

0010267406 BIOSIS NO.: 199698735239
Bifunctional NHS-BAT ester for antibody conjugation and stable technetium-99m labeling: Conjugation chemistry, immunoreactivity and kit formulation
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JOURNAL: Journal of Nuclear Medicine 37 (2): p362-370 1996 1996
ISSN: 0161-5505
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Conjugation chemistry and kit formulated binding of the NHS ester of 6-(4'-(4"-carboxyphenoxy)butyl)-2, 10-dimercapto-2,10-dimethyl-4,8-diazaundecane (NHS-BAT ester) to monoclonal antibodies (MAbs) was investigated. The functionalities of the resulting BAT conjugated and 99mTc-labeled MAbs BW 431/26, MAb 425 and bispecific MDX21 0 (fragment construct) were tested by immunoreactivity and immunoscintigraphy. Methods: The kinetics and chemistry of the conjugation reaction were monitored by high-performance liquid chromatography, size-exclusion chromatography and positive fast-atom-bombardment mass spectra (FAB-MS). The 99mTc BAT-MAbs were tested with various immunoreactivity assays. The biodistribution of 99mTc-BAT-BW 431/26 in rats was compared with directly labeled BW 431/26. Results: At pH 8.5 and 25 degree C, the reactivity of the NHS-BAT ester was high with 90% completion after 30 min. The conjugation yield of 19 mu-M MAb and 228 mu-M NHS-BAT ester amounted to 30%. Higher NHS-BAT ester concentrations afforded higher BAT-to-MAb ratios. According to FAB-MS, the conjugation competing hydrolysis surprisingly occurred at the NHS ring. Almost quantitative 99mTc labeling was achieved after 5 min at 25 degree C. Immunoreactivity of the 99mTc-BAT antibodies showed gt 90% recovery and proved to be insensitive to BAT-to-MAb ratios of up to 10. The 99mTc-BAT-BW 431/26 showed similar organ distribution but revealed less urinary excretion compared with the directly labeled BW 431/26. Immunoscintigraphy with 99m-Tc-labeled and BAT-BW 431/26 and %%%BAT%%%-%%%MAb%%% 425 showed the respective biological function in vivo. Conclusion: According to straightforward conjugation chemistry, the ease of 99mTc labeling and the application of a simple ultrafiltration technique, the NHS-BAT ester represents a nondestructive, universally applicable bifunctional ligand to introduce stable 99Mtc protein binding sites. Kit formulated conjugation/labeling can be performed with little time requirements and laboratory experience.

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DIALOG(R)File 5:Biosis Previews(R)

0009942242 BIOSIS NO.: 199598410075
Activation of human lymphocytes by a monoclonal antibody to B lymphoblastoid cells; molecular mass and distribution of binding protein
AUTHOR: Hardy Britta (Reprint); Galli Michal; Rivlin Eyal; Goren Liz; Novogrodsky Abraham
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JOURNAL: Cancer Immunology Immunotherapy 40 (6): p376-382 1995 1995
ISSN: 0340-7004
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A novel monoclonal antibody (BAT) to the B-lymphoblastoid cell line activates murine lymphocytes and exhibits a striking antitumor activity in mice. In order to evaluate the potential use of this antibody against human cancer, we have investigated its immuno-stimulatory properties on human peripheral blood lymphocytes (PBL). Our findings demonstrate that %%%BAT%%% %%%mAb%%% induces proliferation and cytotoxicity in human PBL against natural-killer-cell-sensitive and natural-killer-cell-resistant tumor cell lines. Interleukin-2 at a low concentration synergizes with %%%BAT%%% %%%mAb%%% in eliciting these effects. %%%BAT%%% %%%mAb%%% binds to human peripheral T cells as revealed by a double-labeling technique using anti-CD3 and %%%BAT%%% %%%mAb%%%. The molecular mass of the antigen recognized by %%%BAT%%% %%%mAb%%% was 48-50 kDa under reducing and non-reducing conditions. This study provides a basis for future experiments to evaluate the use of %%%BAT%%% %%%mAb%%% in the immunotherapy of cancer.
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